Supporting Information

Space constrained stereoselective geometric isomerization of 1,2-diphenylcyclopropane and stilbenes in an aqueous medium

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Table S1. Relative energies of the *cis* and *trans* isomers of guest molecules **1-3** obtained from MD production trajectories.

stilbene	***cis***	***trans***
Vacuum	20.01	0
Water	23.36	0
Benzene	21.20	0
1,2-diphenyl cyclopropane (1)	***cis***	***trans***
Vacuum	10.57	0
Water	10.86	0
Benzene	11.13	0
4.4'-dimethylstilbene (2)	***cis***	***trans***
Vacuum	20.62	0
Water	23.92	0
Benzene	21.78	0
4-propylstilbene (3)	***cis***	***trans***
Vacuum	20.21	0
Water	23.54	0
Benzene	21.39	0

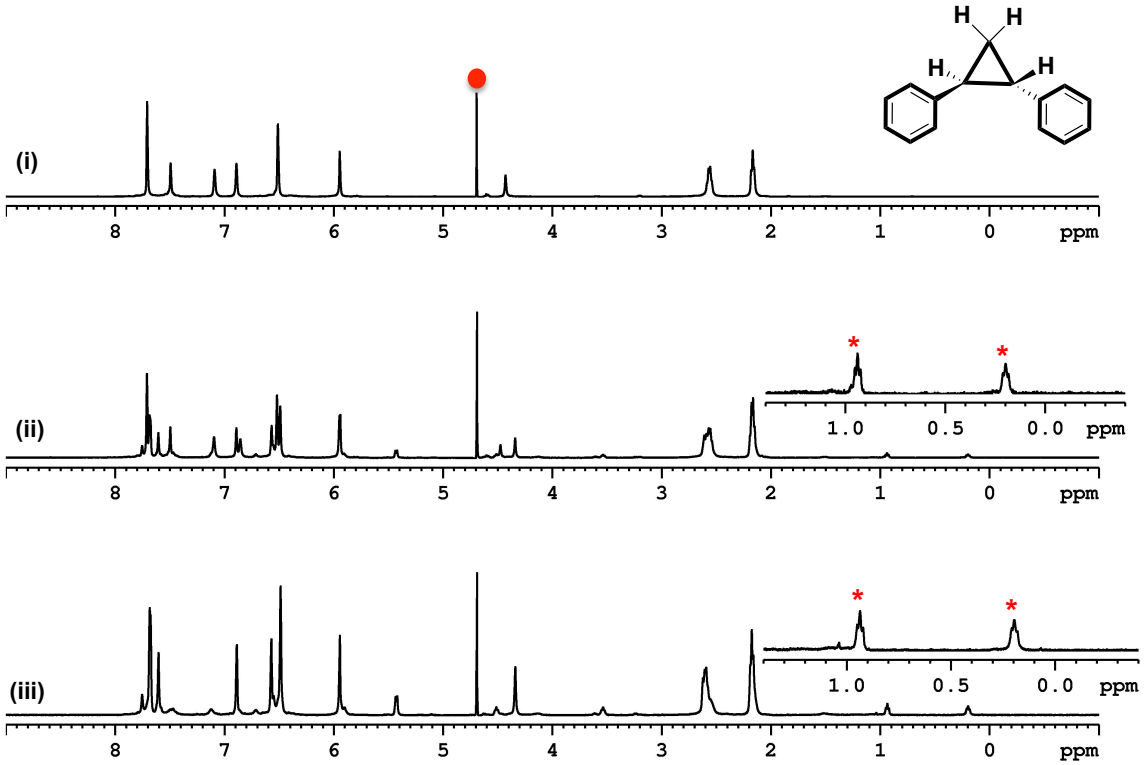


Figure S1. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *trans*-**1**@OA ([OA] = 1 mM), **[1]** = 0.25 mM); (iii) *trans*-**1** @OA ([OA] = 1 mM), [**1**] = 0.5 mM); "*" represent the bound protons of the *trans*-**1** and"●"represent the residual D_2O.

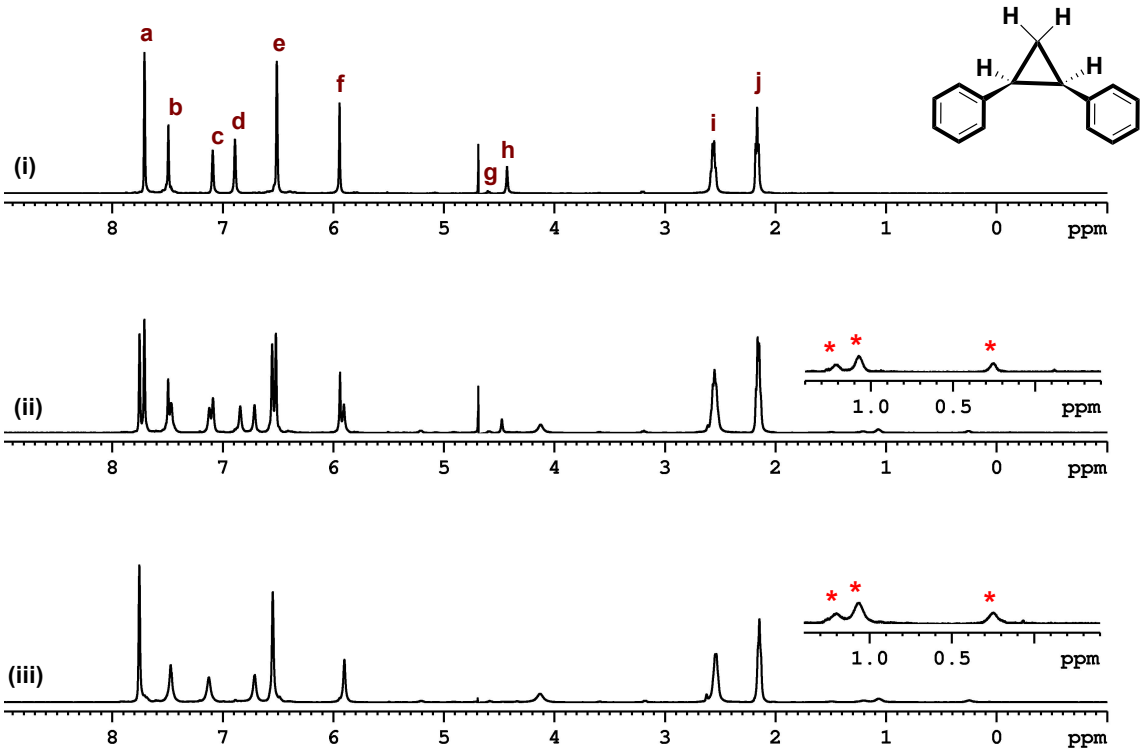


Figure S2. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *cis*-**1**@OA ([OA] = 1 mM), [**1**] = 0.25 mM); (iii) *cis*-**1** @OA ([OA] = 1 mM), [**1**] = 0.5 mM); "*" represent the bound protons of the *cis*-**1**.

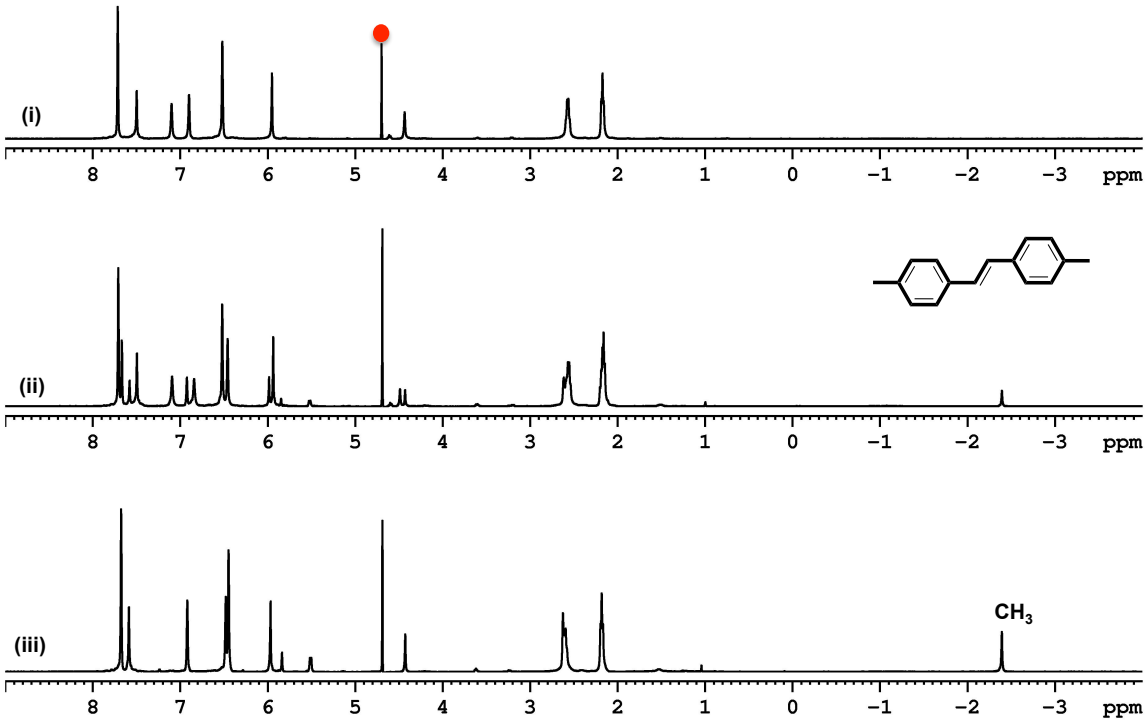


Figure S3. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *trans*-**2**@OA ([OA] = 1 mM), **[2]** = 0.25 mM); (iii) *trans*-**2** @OA ([OA] = 1 mM), [**2**] = 0.5 mM); "●"represent the residual D_2O.

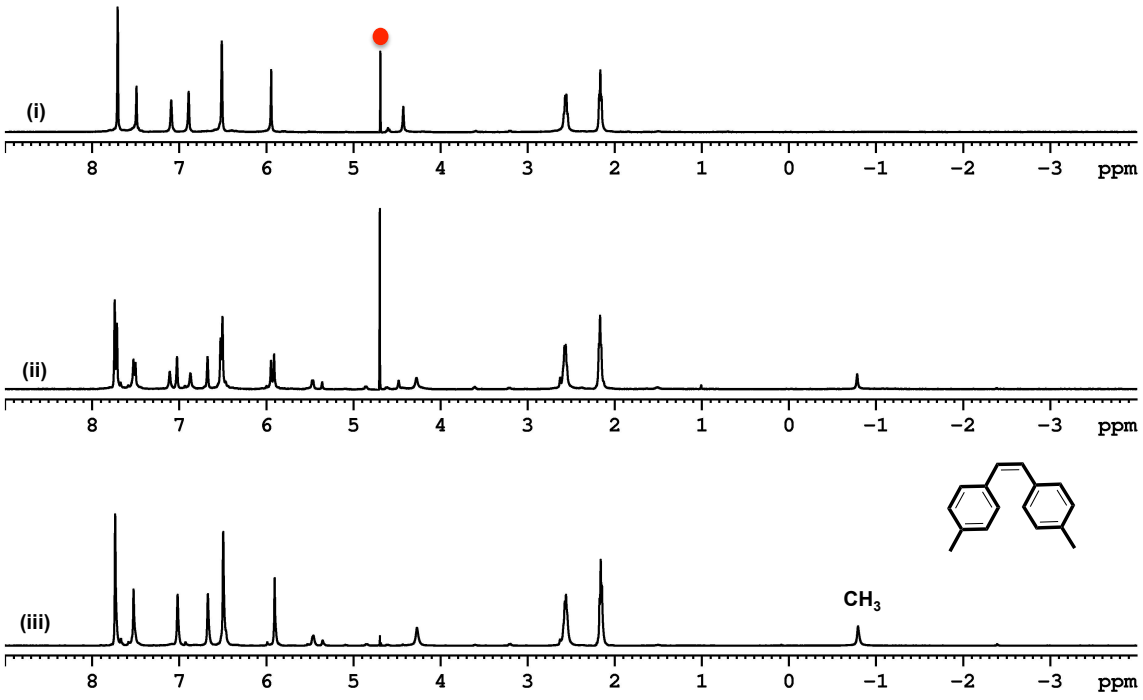


Figure S4. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *cis*-**2**@OA ([OA] = 1 mM), **[2]** = 0.25 mM); (iii) *cis*-**2**@OA ([OA] = 1 mM), [**2**] = 0.5 mM); "●"represent the residual D_2O.

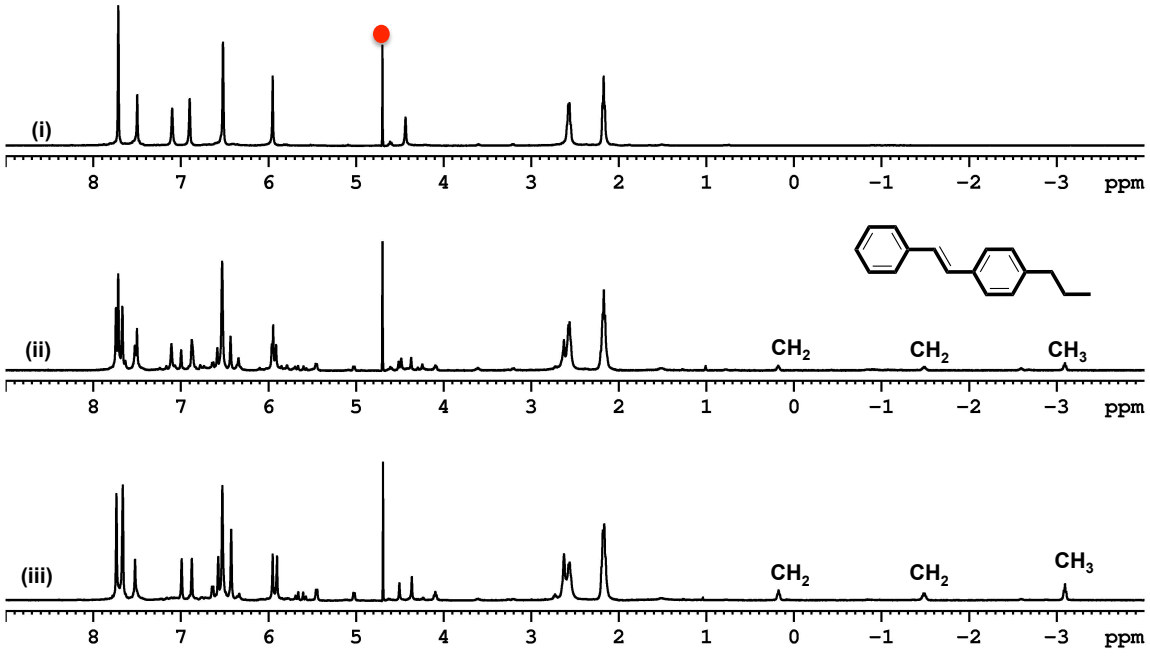


Figure S5. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *trans*-**3**@OA ([OA] = 1 mM), **[3]** = 0.25 mM); (iii) *trans*-**3** @OA ([OA] = 1 mM), [**3**] = 0.5 mM); "●"represent the residual D_2O.

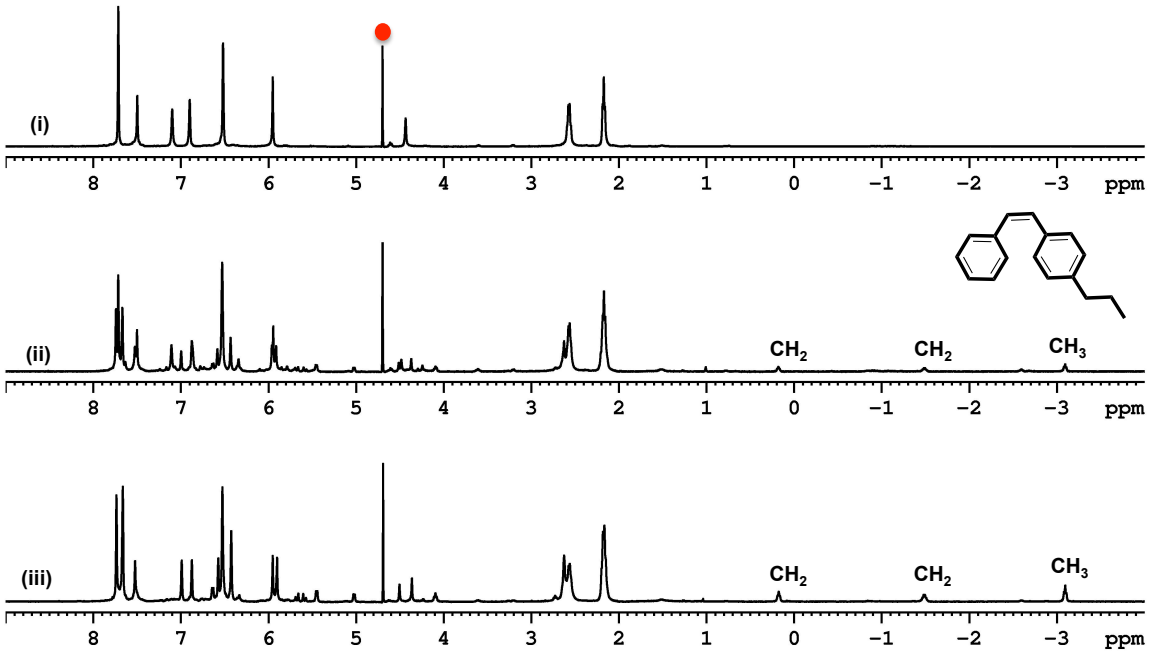


Figure S6. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *cis*-**3**@OA ([OA] = 1 mM), [**3**] = 0.25 mM); (iii) *cis*-**3** @OA ([OA] = 1 mM), [**3**] = 0.5 mM); "●"represent the residual D_2O.

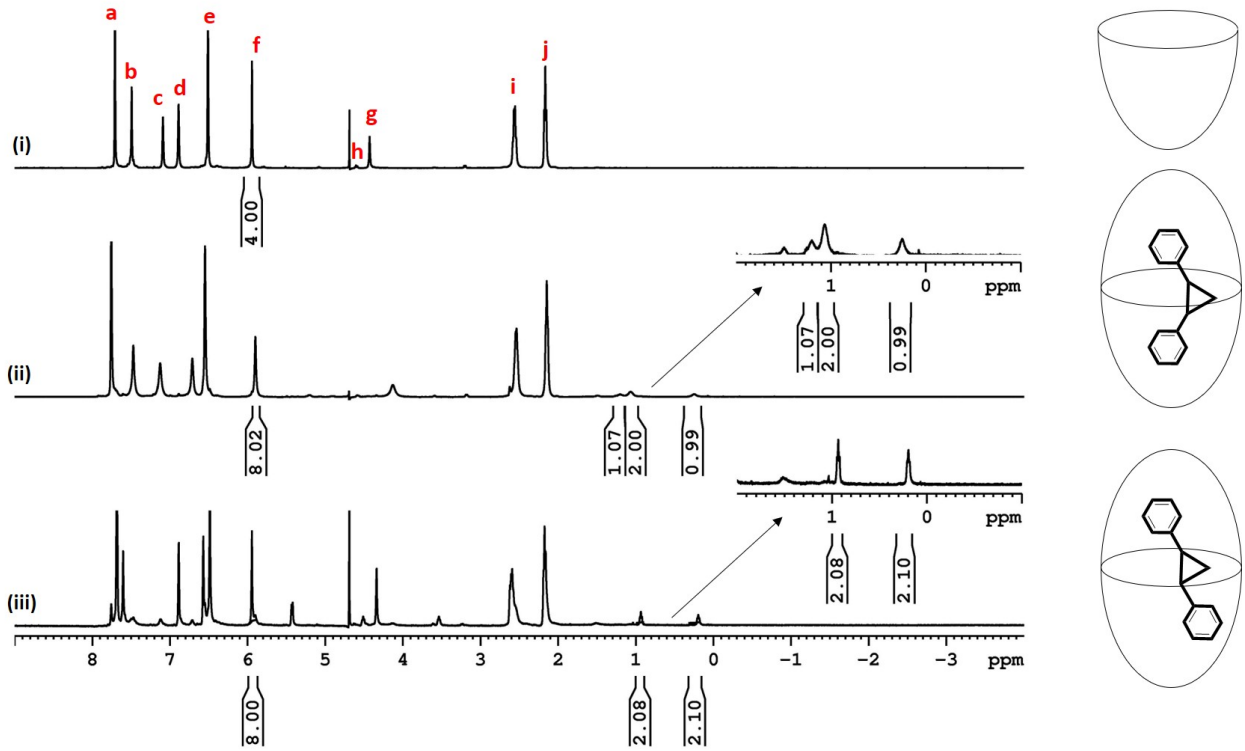
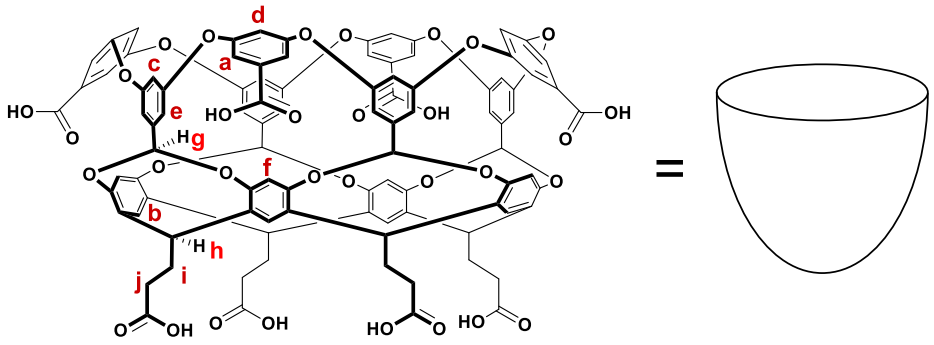


Figure S7. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *trans*-**1**@OA_2; (iii) *cis*-**1** @OA_2 complex.



Note: The ratio of the integration of the H_f of the host OA with respect to cyclopropyl hydrogens is 2:1. The capsule being made up of two OA there are 2 x 4 H_f hydrogens and one guest molecules has 4 cyclopropyl hydrogens. The integration ratio is consistent with 2:1 host-guest complex.

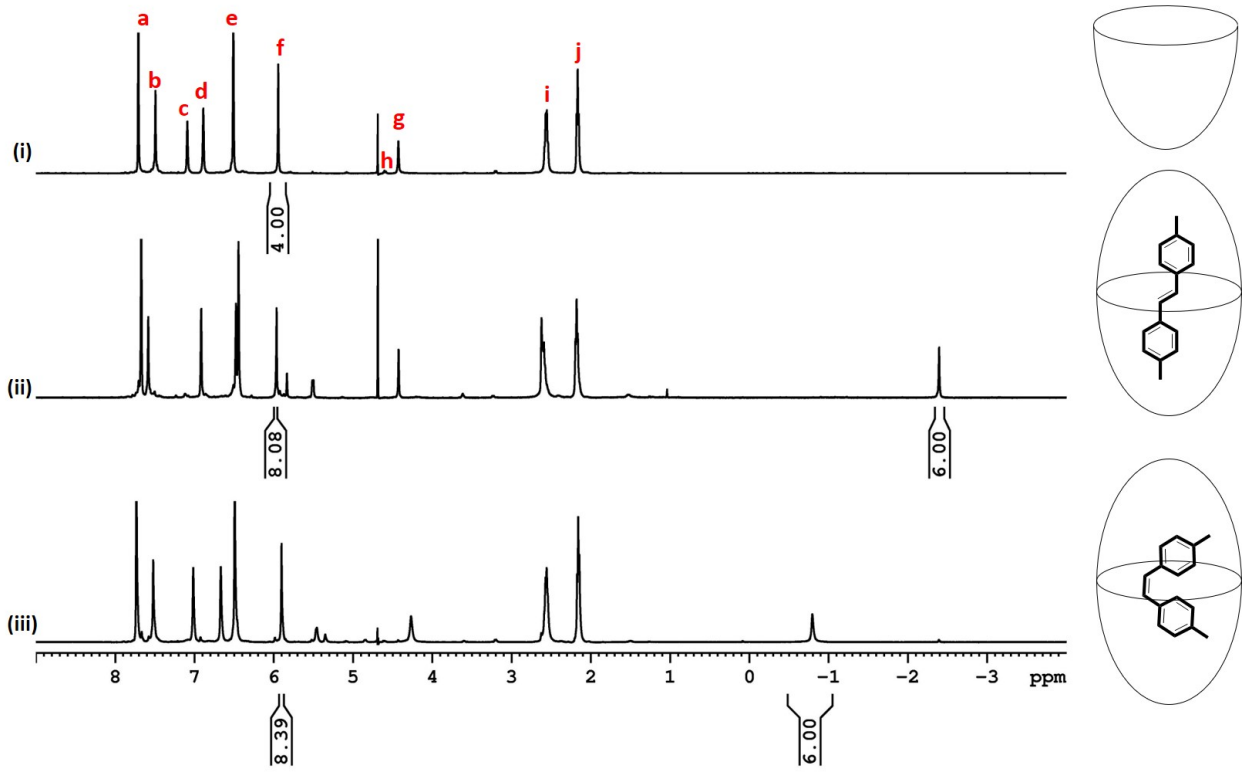


Figure S8. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *trans*-2@OA_2; (iii) *cis*-**2** @OA_2 complex

Note: The ratio of the integration of the H_f of the host OA with respect to methyl hydrogens of the guest is 8:6. The capsule being made up of two OA there are 2 x 4 H_f hydrogens and one guest molecules has 6 methyl hydrogens. The integration ratio is consistent with 2:1 host-guest complex.

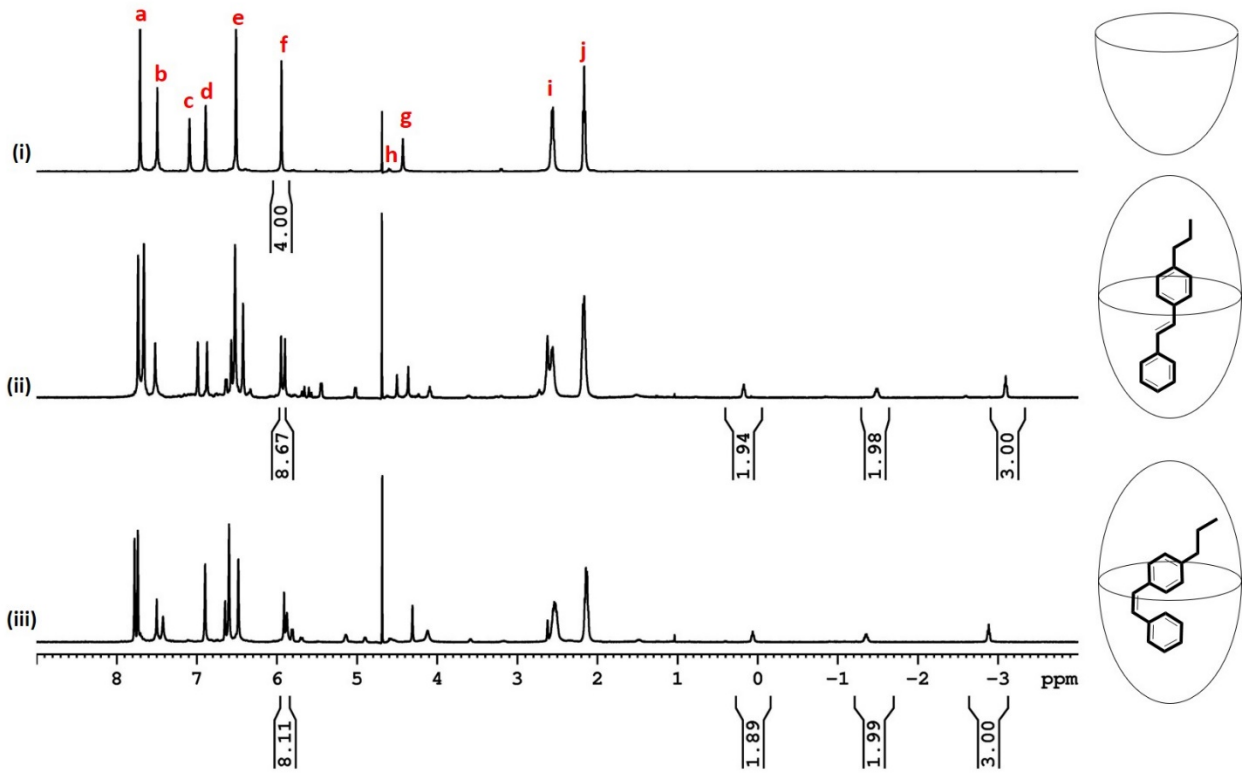


Figure S9. ^{1}H NMR (500 MHz) spectra of (i) OA(1 mM) in 10 mM $Na_2B_4O_7$ buffer/D_2O; (ii) *trans*-**3**@OA_2; (iii) *cis*-**3** @OA_2 complex.

Note: The ratio of the integration of the H_f of the host OA with respect to methyl hydrogens of the guest is 8:6. The capsule being made up of two OA there are 2 x 4 H_f hydrogens and one guest molecules has 6 methyl hydrogens. The integration ratio is consistent with 2:1 host-guest complex. The integration ratios of H_f of the host OA and methylene hydrogens of the guest (8:2 and 8:2) are in agreement with the host-guest ratio of 2:1.

Compound	Diffusion constant (cm^2/s)
OA	1.88×10^{-6}
trans-**1**@OA_2	1.36×10^{-6}
cis-**1**@OA_2	1.45×10^{-6}
trans-**2**@OA_2	1.27×10^{-6}
cis-**2**@OA_2	1.39×10^{-6}
trans-**3**@OA_2	1.37×10^{-6}
cis-3@OA_2	1.30×10^{-6}

Table S2. Diffusion constant of complexes **1**, **2** and **3** with OA by 2D-DOSY NMR.

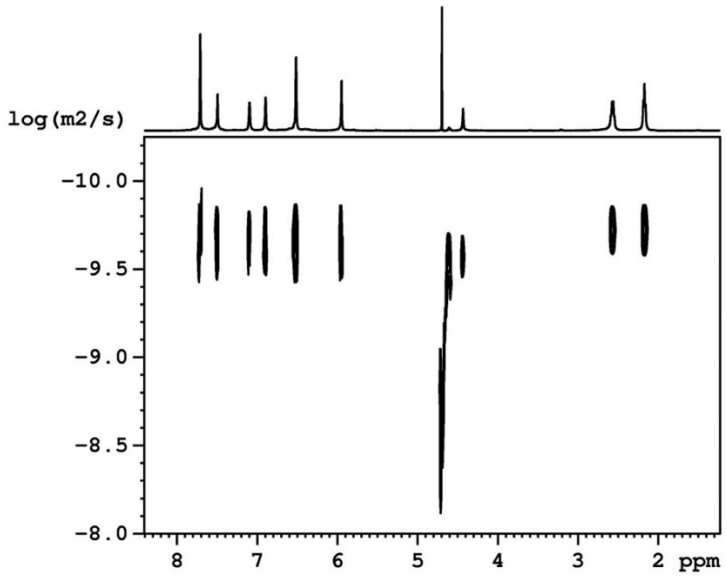


Figure S10. 2D-DOSY spectrum of OA (2 mM) in borate buffer.

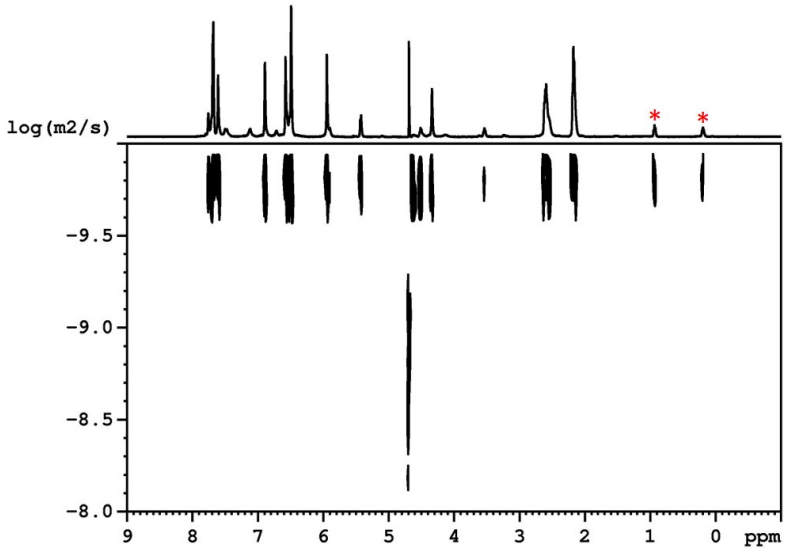


Figure S11. 2D-DOSY spectrum of *trans*-**1**@OA_2 complex.

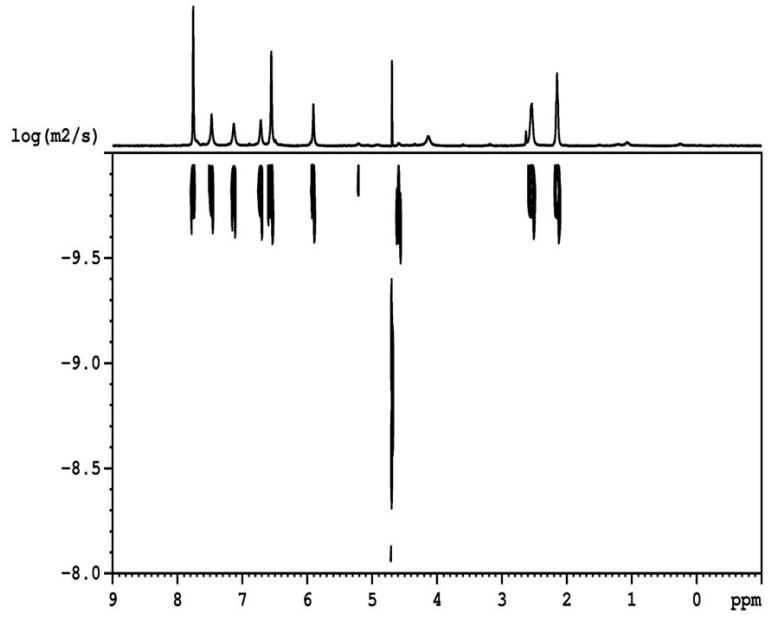


Figure S12. 2D-DOSY spectrum of *cis*-**1**@OA_2 complex.

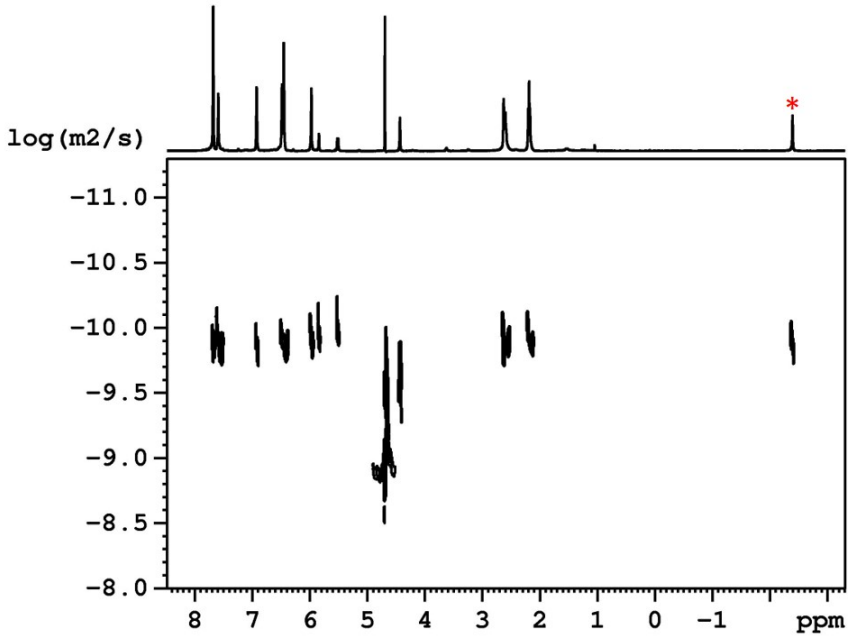


Figure S13. 2D-DOSY spectrum of *trans*-**2**@OA_2 complex.

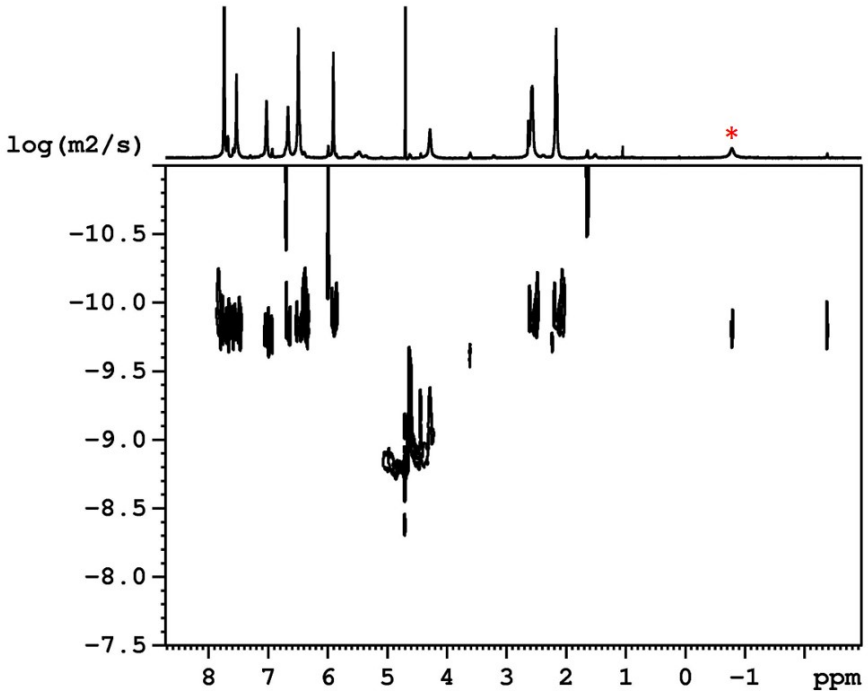


Figure S14. 2D-DOSY spectrum of *cis*-**2**@OA_2 complex.

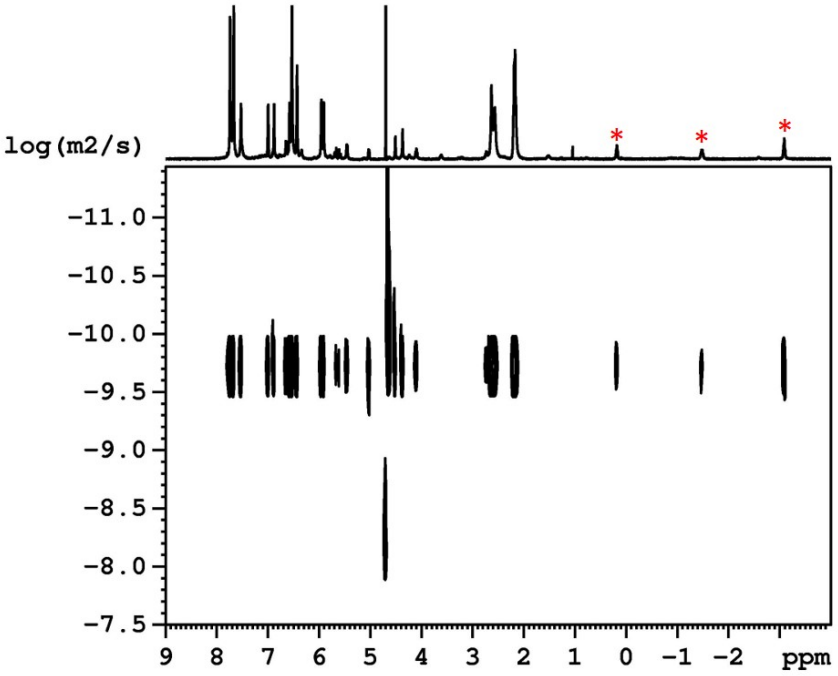


Figure S15. 2D-DOSY spectrum of *trans*-**3**@OA_2 complex.

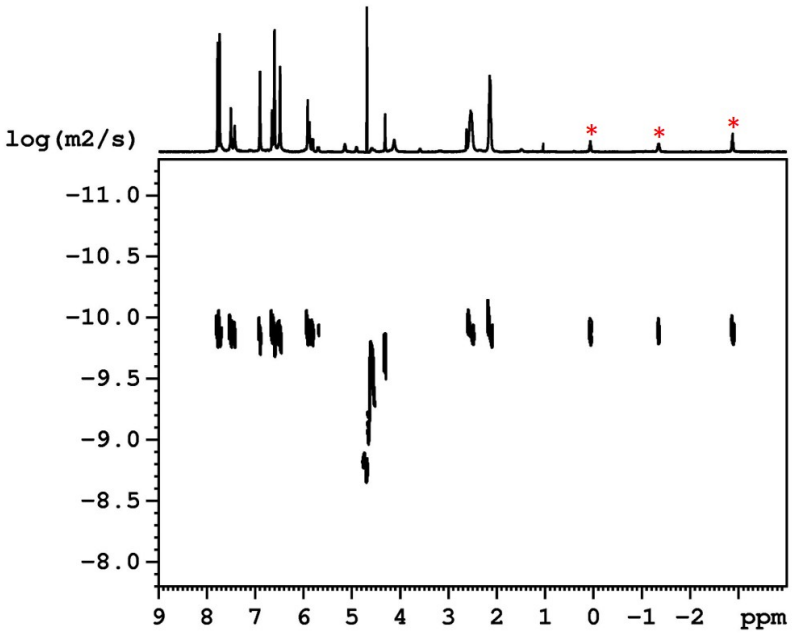


Figure S16. 2D-DOSY spectrum of *cis*-**3**@OA_2 complex.

Compound	**Solution (acetonitrile)[a,b]**	**OA** [a,b]
	trans : cis	***trans : cis***
1,2-diphenylcyclopropane **(1)**	55 : 45	90 : 10
4,4'-dimethylstilbene **(2)**	20 : 80	80 : 20
4-propylstilbene **(3)**	15 : 85	3 : 97

Table S3. Photostationary state mixture of guest molecules in solution and within OA capsule (values quantified by NMR integration)

[a] ratios obtained from photoirradiation of both isomers

[b] values mentioned is the average of 3 trials

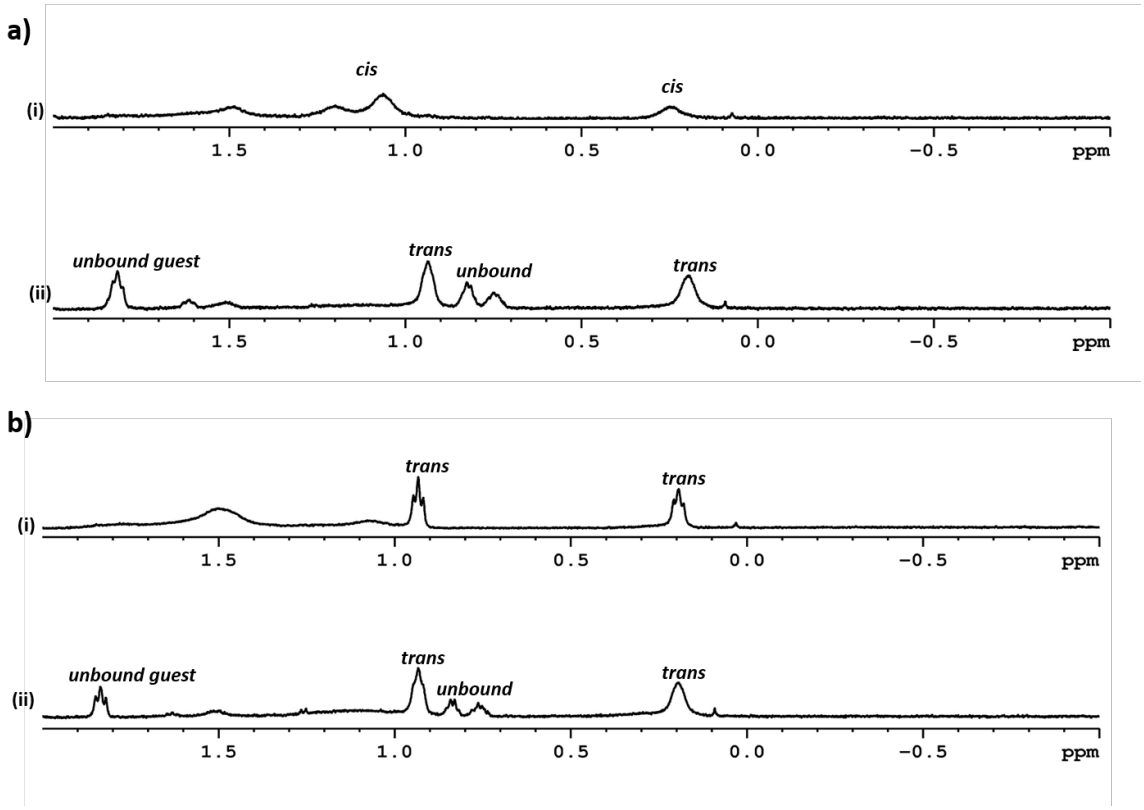


Figure S17. a) Competition experiments between *cis* and *trans* isomers of **1** towards OA capsule. Partial ^{1}H NMR (500 MHz) spectra of (i) 1: 2 complex of *cis*-**1**@OA_2; (ii) upon addition of 0.5 equiv. of *trans*-**1** to (i); b**)** (i) 1: 2 complex of *trans*-**1** @OA_2; (ii) upon addition of 0.5 equiv. of *cis*-**1** to (i).

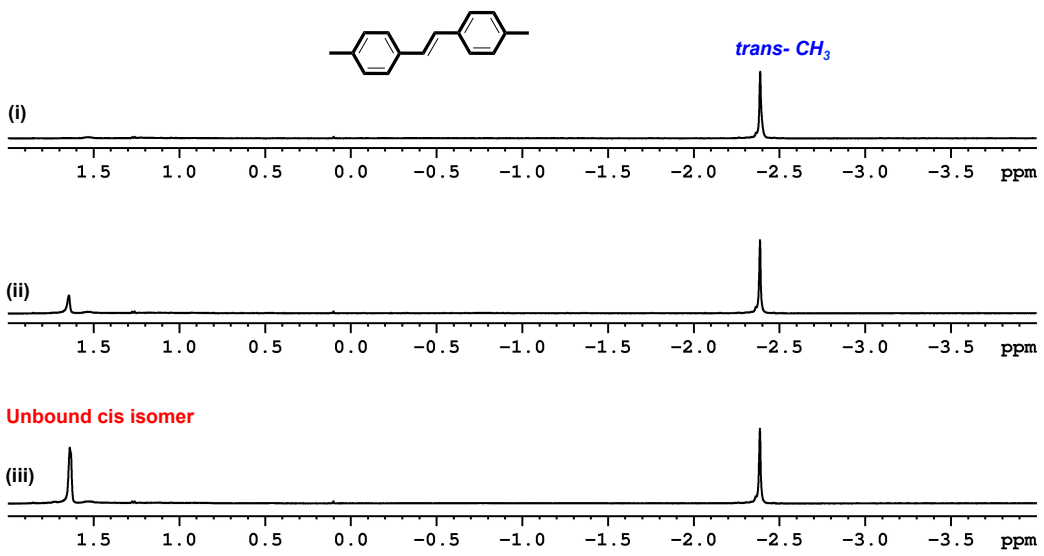


Figure S18. Competition experiments between *cis* and *trans* isomers of **2** towards OA capsule. Partial ^{1}H NMR (500 MHz) spectra of (i) 1: 2 complex of *trans*-**2**@OA_2; (ii) upon addition of 0.25 equiv. of *cis*-**2** to (i); (iii) upon addition of 0.5 equiv. of *cis*-**2** to (i).

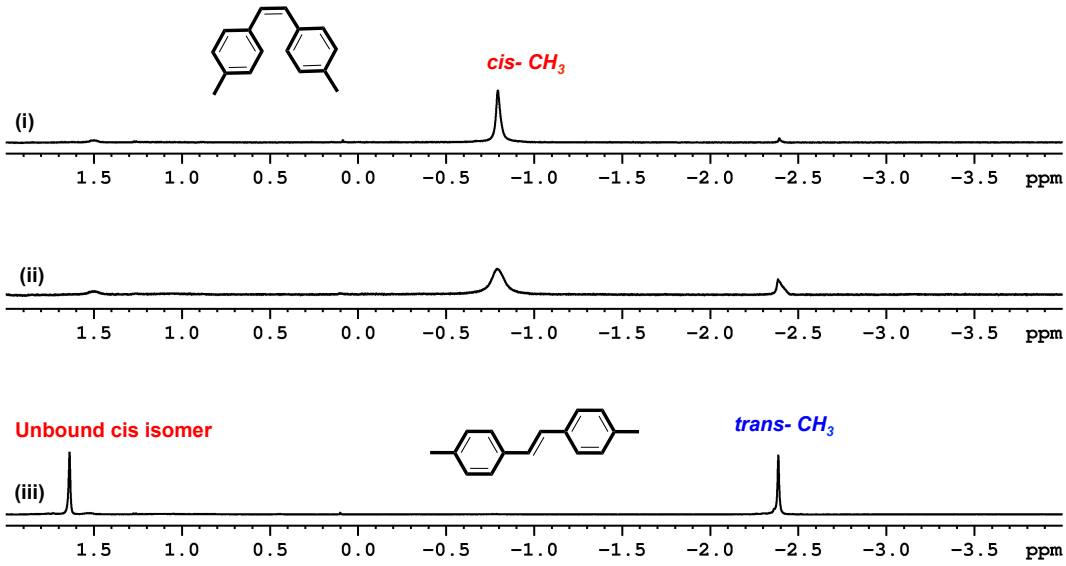


Figure S19. Competition experiments between *cis* and *trans* isomers of **2** towards OA capsule. Partial ^{1}H NMR (500 MHz) spectra of (i) 1: 2 complex of *cis*-**2**@OA_2; (ii) upon addition of 0.25 equiv. of *trans*-**2** to (i); (iii) upon addition of 0.5 equiv. of *trans*-**2** to (i).

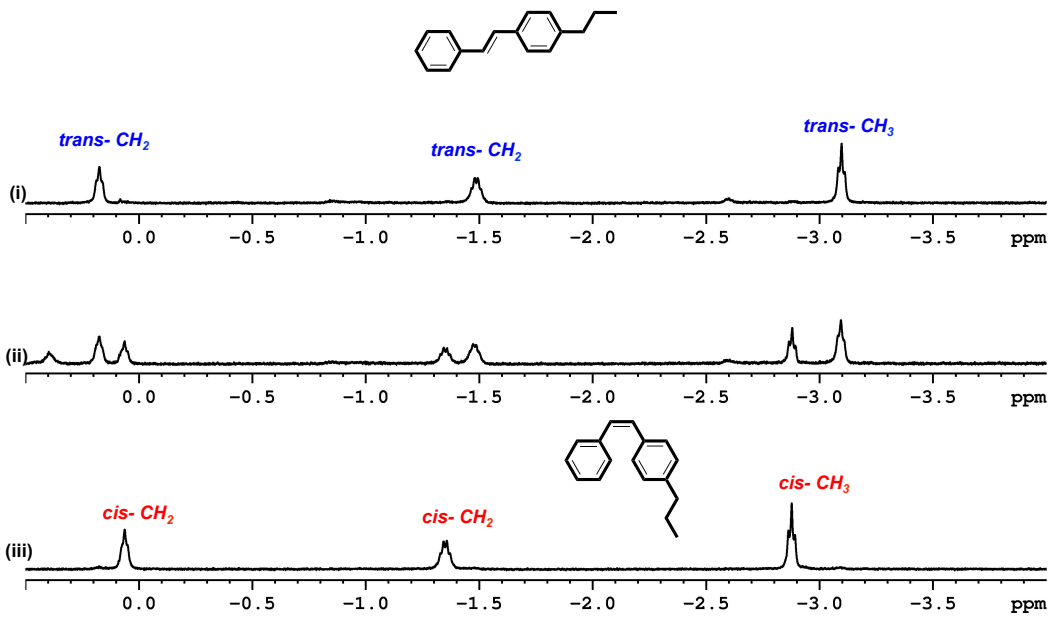


Figure S20. Competition experiments between *cis* and *trans* isomers of **3** towards OA capsule. Partial ^{1}H NMR (500 MHz) spectra of (i) 1: 2 complex of *trans*-**3** @OA_2; (ii) upon addition of 0.25 equiv. of *cis*-**3** to (i); (iii) upon addition of 0.5 equiv. of *cis*-**3** to (i).

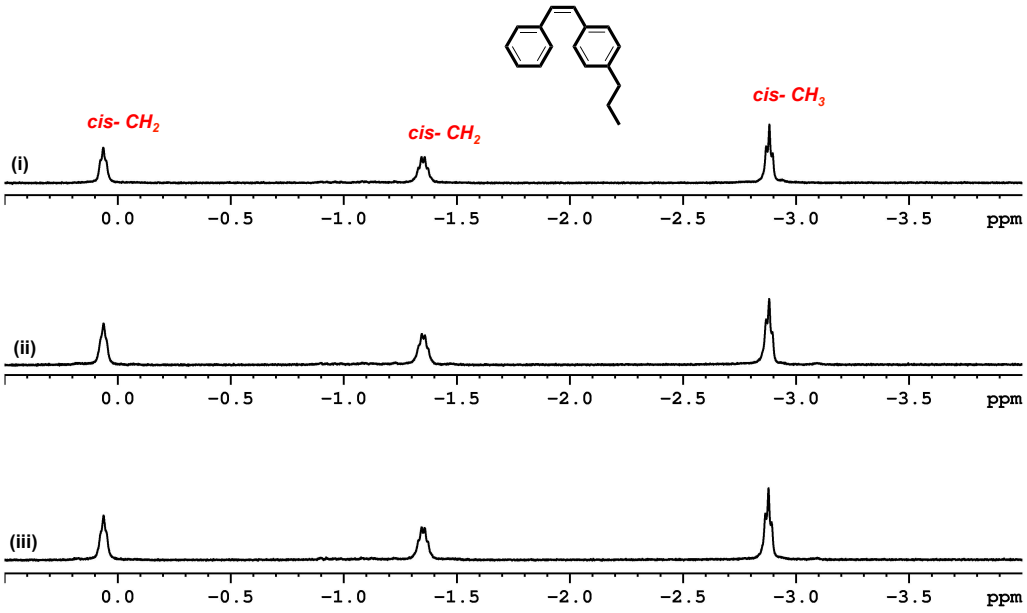


Figure S21. Competition experiments between *cis* and *trans* isomers of **3** towards OA capsule. Partial ^{1}H NMR (500 MHz) spectra of (i) 1: 2 complex of *cis*-**3** @OA_2; (ii) upon addition of 0.25 equiv. of *trans*-**3** to (i); (iii) upon addition of 0.5 equiv. of *trans*-**3** to (i).

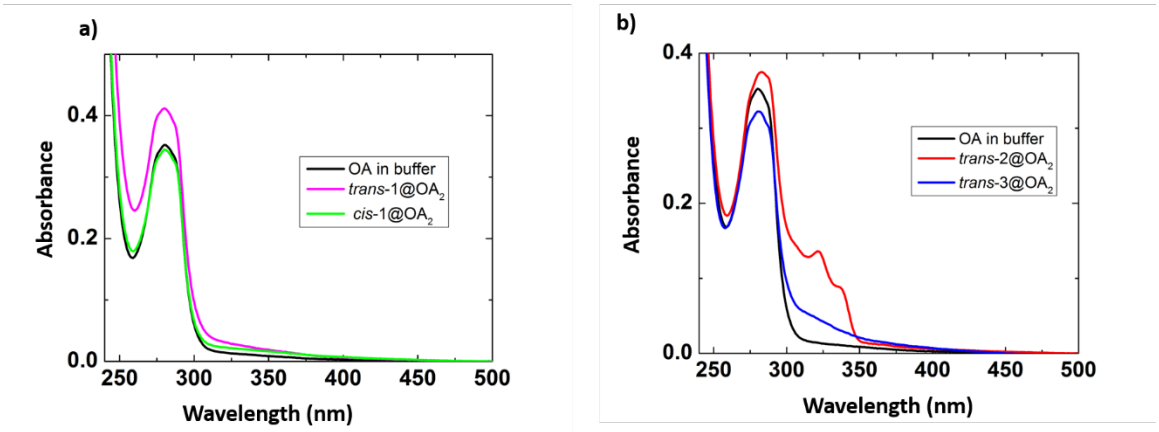


Figure S22. a**)** Absorption spectra of OA in buffer compared with *cis* and *trans* complexes of **1**@OA_2 ; b) Absorption spectra of OA in buffer compared with *trans* complexes of **2** and **3** with OA.

Experimental section

Materials and Methods

The host Octa acid was synthesized following published procedure.[1] *Cis* and *trans* isomers of 4,4'-dimethylstilbene (**2**), 4-propylstilbene (**3**) and 1,2-diphenylcyclopropane (**1**) were synthesized and characterized by reported procedure.[2,3]

General Procedure for guest binding studies probed by NMR

A D_2O stock solution (600 μL) of host OA (1 mM) and sodium borate buffer (10 mM) taken in a NMR tube was titrated with the guest by sequential addition of 0.25 eq of guest (2.5 μL of a 60 mM solution in $DMSOd_6$). The complexation was achieved by shaking the NMR tube for about five minutes. ^{1}H NMR spectra were recorded at room temperature under aerated conditions on a Bruker 500 MHz NMR. 1:2 complex was achieved by 5 μL of guest solution to 600 μL of 1 mM OA host in 10 mM buffer. Competition studies were done by taking *cis* isomer complex in NMR tube and added slowly the *trans* isomer and recorded NMR spectra and vice versa.

Photoirradiation of the complex

1mM concentration of the host-guest complexes (2:1) prepared as above mentioned procedure. The NMR tube was kept in UV-reactor and irradiated using 450 W medium pressum Hg lamp kept in a Pyrex jacket with cold water circulation. Cut off filter (0-54) used to irradiate the stilbene complexes.

Molecular Simulations procedure

OA-guest simulations were performed using the following multistep strategy. In the first step, a three-dimensional structure of OA was taken from our previous work[4] and optimized using the Gaussian09 program.[5] The guest molecules were modeled using the GaussView program package and were optimized without any geometrical constraint at B3LYP[6]/6-31g(d)[7] level using Gaussian09 program. The calculation of RESP charges and the making of the topology files for OA and guest molecules was performed by using Antechamber.[8] Autodock Vina1.5.6 software was used to perform molecular docking to investigate the binding of the guest molecule to the OA.[9] The size of the grid was chosen to cover the OA, and the spacing was kept to 1.00 Å which is a standard value for Autodock Vina. The molecular dynamics (MD) simulations of OA with

guest molecule were performed using the GROMACS4.5.6[10] program utilizing the AMBER03[11] force field. The starting structures were placed in a cubic box with dimensions of 60 × 60 × 60 Å. The shortest distance from the surface of the OA to the edge of the box was 1.0 nm. Electrostatic interactions were calculated using the Particle Mesh Ewald method [12], and a cutoff at 1.2 nm was used for both van der Waals and Coulombic interactions. The box was filled with TIP3P water molecules.[13] To neutralize the system some of the water molecules were replaced with Na and Cl ions. Energy minimization of the OA-guest complex was performed for 3000 steps by the steepest descent method, which resulted in the formation of the starting structure for MD simulations. All the MD simulations were performed for 100 ns. The simulations were carried out with a constant number of particles (N), pressure (P), and temperature (T) (NPT ensemble). To constrain the bond length and angle of the water molecules SETTLE[13]algorithm was used and LINCS[14] algorithm was employed to constrain the bond lengths of the OA. Particle-Mesh Ewald (PME) method was used to calculate the long-range electrostatic interactions. The MD trajectories were computed for each model with a time step of 2 fs. Cluster analysis was performed to derive the most representative structures of the OA. Yasara[15], VMD[16], and Chimera[17] programs were used for visualization and for the preparation of the structural diagrams presented in this study.

References

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